UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

July 1, 2014

MEMORANDUM:

Subject:	Name of Pesticide Product:	MCC 3-Way Fungicide
	EPA Reg. No. /File Symbol:	87845-L
	DP Barcode:	DP 419996
	Decision No.:	486541
	Action Code:	R314
	Submission:	#945584
	E-Sub.	5222
	PC Code:	014504 (Mancozeb: 12.0%) 129106 (Cymoxanil: 4.0%) 023501 (Copper oxychloride: 29.0%)
From:	Byron T. Backus, Ph.D., Toxicologist Technical Review Branch Registration Division (7505P)	Byron T. Backus July-1-2014
To:	Lindsay Roe/Tony Kish RM 22 Fungicide Branch Registration Division (7505P)	M Hash
Registrant:	AGROMARKETING CO, INC	

FORMULATION FROM LABEL:

Active Ingredient(s):		by wt.
014504 Mancozeb (a coordination product of zinc ion and manganese Ethylenebisdithiocarbamate)		12.0%
manganese++	(2.4%)	
zinc	(0.3%)	
ethylenebisdithiocarbamate ion	(9.3%)	
129106 Cymoxanil		4.0%
023501 Copper oxychoride*		29.0%
Other Ingredients:		25.0%
*equivalent to 17.26% elemental copper	TOTAL	100.0%**

**total of 12.0%+4.0%+29.0%+25% on proposed label adds up to 70.0%, not 100.0%.

ACTION REQUESTED: "Please review the proposed first time mixture application for cymoxanil, mancozeb, and copper oxychloride. The submitted studies, as well as the cover letter, can be found on Documentum under e-submission #5222…"

BACKGROUND: The material received by TRB includes a proposed undated label with the signal word WARNING, four acute toxicity studies (acute oral LD_{50} in rats: from OPPIN the MRID is 49229504; acute dermal LD_{50}: 49229505; primary eye irritation: 49229508; primary skin irritation: 49229507) and requests for waiver of the acute inhalation and dermal sensitization studies with submittal of two non-GLP studies (MRID 49229506).

COMMENTS AND RECOMMENDATIONS:

1. The four acute toxicity studies conducted at Product Safety Labs have been classified as acceptable. These studies satisfy the oral LD_{50}, dermal LD_{50}, primary eye and primary dermal irritation study requirements to support the registration of 87845-L.

2. After examining the waiver requests and additional material in MRID 49229506, TRB recommends against waivers for the acute inhalation LC_{50} and dermal sensitization study requirements for the registration of 87845-L.

3. The proposed label for MCC 3-WAY FUNGICIDE includes indications of potential inhalation exposure (statement requiring use of an enclosed cockpit, reference to exposure from drift). The non-GLP inhalation study in MRID 49229506 is not acceptable as supporting data for 87845-L because (among other deficiencies) it was not conducted on the formulation as proposed for registration (Cymoxanil 4% + Mancozeb 12% + Copper oxychloride 29%) but on material identified as "Cuprosate Gold" (containing 64% Mancozeb and 8% Cymoxanil, with no mention of Copper oxychloride). In addition, the particle size (63.1% or more $\geq$5.5 μm) is greater than that specified in the 870.1300 Guidelines ("The MMAD particle size range should be between 1-4 μm.") and it is not evident which of the 3 concentrations (3.2, 4.84 and 5.75 mg/L tested) the particle size data refers to. An inhalation study conducted on the formulation for 87845-L is required.

4. The non-GLP dermal sensitization study in MRID 49229506 is not acceptable as it does not include a positive control assay (from the 870.2600 Guidelines: "The sensitivity and reliability of the experimental technique used should be assessed every 6 months in naïve animals by the use of positive control substances known to have mild-to-moderate skin sensitizing properties."). The registrant has the option of submitting a dermal sensitization study (including an appropriate positive control assay) on the formulation for 87845-L or labeling it as a dermal sensitizer.

5. TRB will make precautionary and first aid labelling recommendations for 87845-L when all acute toxicity study requirements have been satisfied.

Reviewer: Byron T. Backus, Ph.D.
Date: July 1, 2014
Risk Manager (EPA): 22

The following is the Acute Toxicity Data Evaluation Record (DER) for the four acute toxicity studies conducted at Product Safety Laboratories and submitted for EPA File Symbol 87845-L

1. DP BARCODE: 419996				
2. PC CODES: 014504 (Mancozeb); 129106 (Cymoxanil); 023501 (Copper oxychloride)				
3. CURRENT DATE: July 1, 2014				
4. TEST MATERIAL: Cymoxanil 4% + Mancozeb 12% + Copper oxychloride 29% WP, Lot #: 131/072013, described as a pale green powder				
Study/Species/Lab Study # /Date	**MRID**	**Results**	**Tox Cat**	**Core Grade**
Acute oral toxicity (UDP) / rat / Product Safety Labs, Dayton, NJ / Lab Study No. 37148 / October 3, 2013 / OCSPP 870.1100; OECD 425	49229504	Five female rats were orally gavaged with 2000 mg/kg of test material, administered as a 50% w/w mixture in distilled water. None of the rats died. **Oral LD_{50} > 2000 mg/kg.** One rat had diarrhea on day 1, otherwise there were no signs of toxicity. All rats gained weight days 0-7 (15-24 g) and again days 7-14 (5-15 g). No gross abnormalities were observed at necropsy.	III	A
Acute dermal toxicity / rat / Product Safety Labs, Dayton, NJ / Lab Study No. 37149 / October 3, 2013 / OCSPP 870.1200; OECD 402	49229505	5M and 5F rats were dermally exposed for 24 hours to 2000 mg/kg test substance administered as a 75% w/w paste in water. There was no mortality. **Dermal LD_{50} > 2000 mg/kg.** All had yellow staining at the dose site, in some cases through day 14. One F had erythema at the dose site days 1-2. All gained weight days 0-7 (M: 10-17 g; F: 7-14 g) and 7-14 (M: 19-29 g; F: 6-14 g). No gross abnormalities were observed at necropsy.	III	A

Primary eye irritation / rabbit / Product Safety Labs, Dayton, NJ / Lab Study No. 37150 / October 3, 2013 / OCSPP 870.2400; OECD 405	49229508	0.1 mL (0.06 g) instilled in right eye of each of 3 rabbits. Corneal opacity in 2/3 at 24 & 48 hrs, with clearing by day 7. 3/3 eyes had iritis at 24 & 72 hrs, and 2/3 had iritis on day 4 with clearing by day 7. Positive conjunctival effects in all 3 eyes at 24 & 48 hrs, and in 1/3 on day 4. No positive irritation effects on day 7 (2 eyes scored 1 for conjunctival redness) with all scores zero on day 10. MMTS = 25.0 at 24 hrs.	III	A
Primary dermal irritation / rabbit / Product Safety Labs, Dayton, NJ / Lab Study No. 37151 / October 3, 2013 / OCSPP 870.2500; OECD 404	49229507	Each of 3 rabbits received 4-hr dermal semi-occlusive exposure to 0.67 g of a 75% w/w (containing 0.5 g test substance) dry paste mixture with distilled water. At 30-60 minutes all 3 sites scored 1 for erythema and 1 for edema. At 24 hrs all sites scored 1 for erythema, 0 for edema. At 48 hrs 2/3 sites scored 1 for erythema. At 72 hrs all scores were zero. PDII = 0.83.	IV	A

n.d. = not determined; Core Grade Key: A =Acceptable, S = Supplementary, W = Waived, U = Unacceptable, D = Data Gap

The following is the Acute Toxicity Data Evaluation Record (DER) for the non-GLP acute inhalation toxicity study conducted at Toxicology, National Center of Hygiene, Medical Ecology and Nutrition, Sofia, Bulgaria, and submitted for EPA File Symbol 87845-L

1. DP BARCODE: 419996				
2. PC CODES: 014504 (Mancozeb); 129106 (Cymoxanil)				
3. CURRENT DATE: July 1, 2014				
4. TEST MATERIAL: Cuprosate Gold 72 WP: "Cuprosate Gold is a trade name used in Europe for the subject product MCC 3-Way Fungicide." However, the report states that the test material contained 64% Mancozeb and 8% Cymoxanil, with no indication that it contained Copper oxychloride				
Study/Species/Lab Study # /Date	**MRID**	**Results**	**Tox Cat**	**Core Grade**
Acute inhalation toxicity / rat / Toxicology, National Center of Hygiene, Sofia, Bulgaria / no study number / 2000 / OCSPP 870.1300; OECD 403	49229506	Groups of 5M, 5F Wistar albino rats were exposed ("snout only") for 4 hrs to mean concentrations (gravimetrically determined) of 3.2, 4.84 and 5.75 mg/L test material. Particle size: 63.1% or more ≥5.5 µm (concentration at which particle size analysis was done not reported). At 3.2 mg/L all rats survived; at 4.84 mg/L 1/5M and 0/5F died; at 5.75 mg/L 2/5M and 0/5F died. Deaths (including sacrifice in moribund condition) occurred within 24 hours of the end of exposure. LC_{50} = 6 mg/L for males. Clinical signs (all groups): shallow respiration and irregular respiration up to 24 hours post exposure. Individual weight changes reported. Decedents had dark spongy lungs. No abnormalities observed in survivors at necropsy.	(IV)	U

The following is the Acute Toxicity Data Evaluation Record (DER) for the non-GLP dermal sensitization study conducted at Toxicology Laboratory, National Center of Hygiene, Medical Ecology and Nutrition, Sofia, Bulgaria, and submitted for EPA File Symbol 87845-L

1. DP BARCODE: 419996				
2. PC CODES: 014504 (Mancozeb); 129106 (Cymoxanil); 023501 (Copper oxychloride)				
3. CURRENT DATE: July 1, 2014				
4. TEST MATERIAL: TRIPLE FUNGICIDAL COMBINATION – WP (Cymoxanil 4% + Mancozeb 12% + Copper oxychloride 29%), described as a light green powder				
Study/Species/Lab Study # /Date	**MRID**	**Results**	**Tox Cat**	**Core Grade**
Dermal sensitization (Magnusson-Kligman Maximization) / guinea pig / Toxicology Laboratory, National Center of Hygiene, Sofia, Bulgaria / no study number / 2003 / OCSPP 870.2600; OECD 406	49229506	Maximization test with 10 test animals and 5 negative controls. Induction injections for test animals involved 0.2% test material in sterile distilled water and 0.2% test material in 1:1 sterile distilled water: Freund's Complete Adjuvant. Topical applications (induction and challenge) were with 75% test material. Results: all scores zero at 24 and 48 hours following challenge; no indication of a sensitization reaction. However, no results from a positive control study submitted.	n/a	U